

REMARKS

Claims 1-27, 39, 41-46, and 50-53 were previously pending in this Application, and, of these, claims 4-7, 15, 17, 25-27, 39, 41-46, and 50 are withdrawn from consideration by the Examiner at this time. Applicant amends herewith claims 1-4, 12, 13, 15-18, 39, 41-46, 50, and 53. No claims have been added or canceled. Thus, claims 1-27, 39, 41-46, and 50-53 remain pending, and of these, claims 1-3, 8-14, 16, 18-24, and 51-53 are under consideration by the Examiner at this time.

Each of the rejections levied by the Examiner in the outstanding Office Action is discussed in turn below.

Claim Amendments

Applicant amends the claims to a non-invasive method which utilizes contact lenses and eye-drops comprising hyaluronidase and collagenase for treating ophthalmologic conditions. Support for “eye drops” can be found throughout the Application as originally filed (see, *e.g.*, page 17, line 30). Eye drops encompass various forms, such as liquids, sprays, and gels (see, *e.g.*, page 6, line 14, of the Application as originally filed). Support for “non-invasive” can be found on page 4, line 7, of the Application as originally filed. It is generally understood from the present Application that “non-invasive” excludes methods which require surgery (see, *e.g.*, page 4, lines 26-27). It is also generally understood from the present Application that eye drops are topically applied to the eye of a subject in a non-invasive manner.

Applicant further amends the claims to recite that the ophthalmologic condition is a condition involving an error in the refraction of the eye. Support for this amendment can be found on page 4, lines 12-14, of the Application as originally filed.

Applicant further amends the claims to recite that the treatment results in a correction of the ophthalmologic condition. Support for this amendment is can be found in original claims 19-21.

No new matter has been added to the Application by the present Amendment.

Rejection under 35 U.S.C. § 112

The Examiner has rejected claim 12 under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner indicates the word “other” in “other enzymes” renders claim 12 indefinite. Applicant removes the word “other” from claim 12, as well as from withdrawn claims 39, 41, 42, and 46. In light of this amendment, Applicant respectfully requests this rejection of claim 12 be withdrawn.

Rejection under 35 U.S.C. § 103

The Examiner has rejected claims 1-3, 8-14, 16, 18-24, and 51-53 under 35 U.S.C. § 103(a) as being unpatentable over EP 0608341 (hereafter “Harris”) in view of U.S. Patent Application Publication 2005/0080484 (hereafter “Marmo”) and further in view of U.S. Patent 6,610,292 (hereafter “Karageozian”).

Specifically, the Examiner points to Harris as teaching methods for accelerating corneal reshaping involving the application of hyaluronidase and a contact lens. While the Examiner indicates Harris discloses collagenase, the Examiner concedes Harris does *not* teach the claimed combination of hyaluronidase and collagenase. The Examiner further indicates that Harris does *not* teach the use of a polymer such as cellulose in the formulation or teach the treatment of presbyopia.

The Examiner points to Marmo to remedy certain deficiencies in Harris. Specifically, the Examiner indicates Marmo teaches methods and devices for improving vision comprising a lens. The Examiner points to Marmo as teaching treatment of visual deficiencies such as presbyopia. The Examiner further points to Marmo as teaching use of a gel comprising, for example, a cellulosic component. However, the Examiner concedes that Marmo, like Harris, does *not* teach the claimed combination of hyaluronidase and collagenase.

The Examiner also points to Karageozian to remedy certain deficiencies in Harris and Marmo. The Examiner finds Karageozian teaches a method for treating ophthalmic disorders using hyaluronidase and teaches that other enzymes, such as collagenases, may be used as alternatives to hyaluronidase. However, the Examiner again concedes that Karageozian, like Harris and Marmo, does *not* teach the claimed combination of hyaluronidase and collagenase.

Despite the fact that neither Harris, Marmo, nor Karageozian teach the claimed combination of hyaluronidase and collagenase, the Examiner still finds the claimed combination obvious. Specifically, the Examiner posits that it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ enzymes such as hyaluronidase or collagenase, or combinations thereof, in the treatment of ophthalmologic conditions as taught by Karageozian using the method of Harris.

Applicant respectfully disagrees with the Examiner's conclusions and respectfully submits that the number of references needed to make this obviousness rejection, compounded with the fact that none of these references actually teach, suggest, or provide the motivation to arrive at the claimed combination, is strong evidence that the claimed invention is *not* obvious.

Moreover, Applicant submits it appears that the Examiner is cherry-picking from these references for the purpose of making the present rejection with the benefit of hindsight based on the teachings of the present Application. This is impermissible when evaluating obviousness. As stated by the Federal Circuit in *Orthopedic Equipment Co., Inc. v. United States*, 217 U.S.P.Q. 193, 199 (Fed. Cir. 1983), "It is wrong to use the patent in suit [here the patent application] as a guide through the maze of prior art references, combining the right references in the right way to achieve the result of the claims in suit. Monday morning quarterbacking is quite improper when resolving the question of obviousness in a court of law [here in the U.S. Patent and Trademark Office]." Similarly, the Federal Circuit stated in *In re Fine*, 5 USPQ2d 1600 (Fed. Cir. 1988) that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." Therefore, Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness based on the prior art.

However, solely in an effort to expedite prosecution, Applicant further amends the claims to more closely encompass Applicant's marketed product, Yolia Health's KDMIT[™] treatment. This non-invasive treatment involves the use of contact lenses and an eye drop formulation comprising an effective amount of hyaluronidase and collagenase, which, when used together, safely shape a patient's cornea leading to improved vision. This treatment was first approved for commercial use in Mexico in 2008 and has been clinically piloted with more than 125 patients to date, with an average near-vision efficacy exceeding 73% (based on the Jaeger Scale for near vision acuity

efficacy standard of improving vision to J5-J3). For example, after 7 days of treatment patients are able to stop using their glasses and corrective lenses for up to several weeks at a time before retreatment is needed. Patients experienced no distance vision loss as a result of this treatment. In fact, several patients gained distance vision acuity after the treatment was completed. Moreover, no adverse affects have occurred as result of this treatment. The claimed enzymatic treatment is an unexpected improvement on other more traditional methods, such as Ortho-K. According to Dr. Stuart Grant, a prominent California optometrist and pioneer of Ortho-K, Yolia Health's KDMI™ treatment will be a "game-changing breakthrough" because it leverages the proven therapeutic power of traditional Ortho-K, yet extends the time of efficacy from hours to months (see Yolia Heath's August 4, 2010 News Release, enclosed herewith as **Exhibit A**). Applicant anticipates that, upon approval of the KDMI™ treatment in the United States and other countries, the claimed method will have a dramatic impact on the global eye care market.

Applicant thus submits that the claims, as amended, are not obvious in view of the cited references. The claims, as amended, are directed to a non-invasive method for treating an ophthalmologic condition using contact lenses and eye drops comprising a combination of hyaluronidase and collagenase. In contrast, *all* of the references cited by the Examiner, from Harris, to Marmo, to Karageozian, describe to a greater or lesser extent invasive techniques, and *none* of the references teach, suggest, or provide motivation to arrive at the claimed combination of hyaluronidase and collagenase. Marmo describes incising the cornea and inserting a lens under the incision in order to correct vision (see, *e.g.*, Figures 6A-6C of Marmo). While Harris mentions the use of eye drops (see, *e.g.*, paragraph [0013] of Harris), and Karageozian mentions topical application (see, *e.g.*, column 6, line 47, of Karageozian), all of the working examples of Harris and Karageozian teach injecting a hyaluronidase solution into the eye (see, *e.g.*, the Examples of Harris and Karageozian). Applicant considers the combined focus of these references on invasive treatments as a clue to the general inclination and practice of the skilled artisan at the time of filing the present Application. Thus, Applicant submits one skilled in the art, acquainted with Harris, Marmo, and Karageozian, would *not* be motivated to develop a non-invasive method, as presently claimed, but rather would be motivated to further pursue the espoused invasive methods. Moreover, Applicant submits, one skilled in the art, acquainted with Harris, Marmo, and Karageozian, would

not be further motivated to develop a non-invasive method using a combination of hyaluronidase and collagenase, as presently claimed.

The evidence submitted herewith further supports this finding of non-obviousness. Researchers have worked for many years to develop orthokeratology for long-term correction of refractive error. As demonstrated by the evidence submitted herewith, Applicant has found that a combination of contact lenses and an enzymatic formulation comprising hyaluronidase and collagenase is more effective in treating vision problems than traditional orthokeratology.

For all of the above reasons, Applicant submits Harris in combination with Marmo and Karageozian does not render claims 1-3, 8-14, 16, 18-24, and 51-53 obvious. Applicant respectfully requests that this § 103 rejection be withdrawn.

In view of the above Amendment and Remarks, Applicant believes the pending Application is in condition for allowance.

Applicant believes no fee is due with this Response. However, if a fee is due, please charge it to our Deposit Account No. 23/2825, under Docket No. O0327.70000US00, from which the undersigned is authorized to draw.

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Respectfully submitted,

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